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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,275	COLEMAN ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

S. A.M.

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20,23,60 and 61* is/are pending in the application.

4a) Of the above claim(s) *1,2,11,14-18,20 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-10,12,13,60 and 61* is/are rejected.

7)☒ Claim(s) *3-10,12,13,60 and 61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§.119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8-2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Priority

1. This application is a continuation of 08/390740, filed 2/17/95. Thus, the effective filing date of this application is 2/17/95.

Election/Restrictions

2. Applicant's election with traverse of invention III or IV in the paper filed 8/20/03 is acknowledged. Applicant's assumption that groups III and IV were meant to be different based on whether the claims were directed to SEQ ID NO: 1 or SEQ ID NO: 3 was correct. The examiner regrets the omission from the restriction requirement and thanks applicant for making the election with traverse of the invention as it relates to SEQ ID NO: 3, nucleic acids encoding a polypeptide of SEQ ID NO: 4. The traversal is on the ground(s) that there would be no undue burden for the Examiner to fully examine the elected group as well as the claims that include polypeptides, antibodies, methods for detection of nucleic acids, and methods for screening a compound for effectiveness as an agonist or antagonist, in view of the fact that a "complete examination" of this Group has occurred in the parent application, and applicant has provided "a very thorough search" for all of the inventions. This is not found persuasive because first, a thorough examination of the claims of record in the instant application has not been provided, as most of the claims have been extensively amended herein. Further, applicant's argument that there would be not additional burden on the examiner to search and examine six additional separate and distinct groups is not supported by any reasoning that would overcome the fact that each of these would require separate search of the prior art, and separate analysis for enablement,

utility and description, for example. The requirement is still deemed proper and is therefore made FINAL.

With regard to the methods of detection of polynucleotides, which are related to the instant invention as a product and a process of use, in the event of the finding of allowable subject matter, rejoinder will be considered as appropriate.

In cases as in the instant case, where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to

retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

3. Claims 60 and 61 have been added and are drawn to subject matter within the elected group. Therefore claims 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 60 and 61 are under examination herein.

4. It is noted that claims 3-10 all depend from non-elected claims 1 and 2. Prior to allowance of any of claims 3-10 they will be required to be amended so that they do not depend from non-elected claims.

Drawings

5. The newly filed drawings have been entered. All drawings filed are approved for examination.

Information Disclosure Statement

6. The information disclosure statements filed 10/25/01 and 8/22/02 have been considered. A number of references on the later filed 1449 were lined through because they are duplicates of references listed on the first filed 1449. All of the listed references have been considered.

Specification

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s):

(A) There are two amino acid sequences recited in figures 3A-3C that are not identified by proper SEQ ID NO in the amended description of the drawings. Namely, the sequences identified in the figure as 226152 and 223187 are not identified with proper sequence identifiers.

(B) The CRF transferred from the parent application and the paper copy of the sequence listing filed 10/25/01 are not identical. SEQ ID NO: 1 in the paper copy has 291 nucleotides (ending with "CCA") while the sequence in the CRF has 289 nucleotides, ending with "AGC."

In order to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825), Applicant must submit an amendment which either corrects the description of the drawings or adds sequence identifiers to the figures.

8. The disclosure is objected to because of the following informalities: the specification on page 15 states that the sequences of the coding region of PANEC-1 and PANEC-2 are shown in figure 1, yet only a single coding region is show in figure 1 (that of PANEC-1).

9. Further, the disclosure at pate 16 refers to figures 2 and 3, but these figures are not longer in the file per se as they have been replaced with figures 2A-2B and figures 3A-3C, respectively.

Appropriate correction is required.

10. The amendment to the title is approved. A request will be placed for the title to be updated in the patent application monitoring system.

Claim Rejections - 35 USC § 112- New Matter

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-10, 12, 13, 60, and 61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitations of "has an insertion of deletion of 1-5 amino acids as compared with SEQ ID NO: 4" and "has one or more amino acid substitutions as compared with SEQ ID NO: 4, and has the amino acid sequence of SEQ ID NO: 4 at amino acids 1, 4, 6, 7, 10, etc..." in claim 1 (from which claims 3-10 depend) and in claim 12 appear to represent new matter.

In the remarks filed with the amendment entering these limitations, applicant points to page 8, lines 1-2 as stating "The DNAs which encode PANEC-1 and PANEC-2 may also include allelic or recombinant variants and mutants thereof (p. 11 of the paper)." It is noted that this statement is not located on page 8 of the specification, but instead on page 7, lines 19-20. Nonetheless, it is agreed that this statement generically provides support for the language "allelic or recombinant variant" from a new matter perspective. However, the specific limitations

repeated in this rejection are not adequately supported by this recitation as this recitation does not discuss the length of any possible deletion, nor does this recitation discuss any particular amino acids that are necessary to be retained in a variant of SEQ ID NO: 4.

Applicant further points to the specification at figures 3A, 3B, and 3C as providing support for the various limitations in the amounts and types of insertions, deletions and substitutions. Applicant states that Figure 3A, 3B, and 3C compare PANEC-2 (SEQ ID NO: 4) to its three closest prior art molecules at the time of the invention, namely MIP-1a, MIP-1b, and. RANTES. Figure 3 also compares SEQ ID NO: 4 (referred to therein as 226252) to MCP-1, MCP-2, MCP-3, and instant SEQ ID NO: 2, referred to in Figure 3 as 223187. The remarks state that the numbers utilized in the instant claims are "mathematical calculations of sequence selections" based on figures 3A, 3B, and 3C. However, there does not appear to be basis for these calculations in the specification.

Applicant points to page 7, lines 6-7 as supporting the language "has an insertion or deletion of 1-5 amino acids as compared with SEQ ID NO: 2." It is noted that the sequence recited in the pending claims is SEQ ID NO: 4, not SEQ ID NO: 2. Nonetheless, this portion of the specification defines the terms "oligonucleotide" and polynucleotide "fragment", "portion" or "segment" and does not appear to discuss deletions of 1-5 amino acids in polypeptides. The previous page discusses amino acid insertions, deletions and substitutions, and states that "Guidance in determining which amino acid residues may be replaced, added, or deleted without abolishing activities of interest, such a cell adhesion and chemotaxis, may be found by comparing the sequence of the particular PANEC with that of homologous cytokines and minimizing the number of amino acid sequence changes made in regions of high homology (p. 6,

fifth paragraph)." This language does not discuss a number of amino acids that may be inserted or deleted in this "minimizing" process, and thus, the claims are rejected as containing new matter over this recitation.

Applicant points to this same section in the fifth paragraph of page 6 as support for the amendments which recite the long listing of amino acids that must be common to the variants, suggesting in the remarks that "by counting the number of amino acid changes between PANEC-2 with respect to all three of the prior art MCPs disclosed in the specification, further stating that the specification provides guidance for and supports identification of specific amino acid residues of PANEC-2 which should be retained in a variant, "i.e., wherein 2 of the three MIPs and/or RANTES ("homologous cytokines") have the same amino acid at a specific location...as PANEC-2, and by allowing only sequence variation at residues where PANEC-2 differs from at least 2 of the three MIPs and/or RANTES." This is not persuasive.

The generic guidance in the specification does not make readily apparent the specific guidance given in the remarks. The generic guidance repeatedly cited by applicant is vague at best, referring to "homologous cytokines" but not stating what degree of homology is required, and also guiding one to "minimize" the number of amino acid changes in regions of "high homology," but never qualifying these relative phraseologies with actual limitations. The guidance provided in applicant's remarks is quite detailed, the details of which do not appear to be based on the specification but on criteria that are not recited in the specification. Furthermore, applicant's own guidance on page 12 of the response conflicts, referring to counting the amino acid changes between the MCPs and SEQ ID NO: 4 in the beginning of the paragraph, and then at the latter half of the paragraph referring to comparisons of PANEC-2 with the MIPs and/or

RANTES. Nonetheless, the specification does not give any guidance as to why one would preferentially compare SEQ ID NO: 4 to any of the sequences given in figure 3, and indeed, in Figure 3, SEQ ID NO: 4 is compared to all of these sequences, or so it appears, based on the shading that overlaps with all of the sequences at some positions (for example at amino acid numbered 61 of the "majority").

Most of applicant's selections of the amino acid residues in claims 1 and 12 appear to follow the "two of three" rule set forth in the remarks with regard to MIPs and/or RANTES. It does not apply to all of the residues recited in claims 1 and 12, however, for example, required residue 50 in the PANEC-2 molecule is a glutamic acid (E), yet none of the other cytokines appear to share this residue at the aligned position (see Figure 3B). Furthermore, the "two of three rule," as noted, does not appear to be supported in the specification. It is not clear why one would choose, based on the guidance in the specification to "minimize" differences with these three sequences as opposed to the other four sequences given in Figure 3. Instant SEQ ID NO: 4 is compared to seven total sequences in Figure 3, and there is no clear guidance in the specification as to when describing a "variant" of SEQ ID NO: 4 one would look only to three of these seven sequences for guidance. For example, at position 47 of instant SEQ ID NO: 4 shares a serine residue with the three MCP molecules and with SEQ ID NO: 2. However, this is not an amino acid position recited in the "required" amino acids of claims 1 and 12. Given the general guidance in the specification, the instant amendments reciting particular numbers of insertions or deletions and reciting specific amino acid numbers are not supported.

Because no specific basis for these limitations was identified in the specification, nor did a review of the specification by the examiner find any basis for the limitations, the claims are rejected as incorporating new matter.

Further, turning to claims 60 and 61, in particular, in these claims the negative limitations "is non-genomic" and "without introns" appear to be new matter. In applicant's remarks at page 14, applicant suggests that these limitations are supported as "the negative" of the definition in the specification on page 10, lines 2-3. This portion of the specification reads "The hybridization probes of the subject invention may be derived from the nucleotide sequences of the SEQ ID NO:1 or SEQ ID NO:3 from genomic sequences including promoters, enhancer elements and introns of the respective naturally occurring panecs (specification p. 10, lines 1-3)," thus clearly setting forth that applicant intends for the hybridization probes of their invention to encompass genomic DNA, specifically reciting introns as included within the genus of hybridization probes. As noted by MPEP 2173.05(i),

"Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

In this case, there is not absence of a positive recitation, but instead, there is presence of a positive recitation, and no suggestion within the specification of the negative limitations. Since

no basis for the negative limitations has been identified, the claims are rejected as incorporating new matter.

Claim Rejections - 35 USC § 101/112 1st, Lack of Utility

12. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 1-10, 12, 13, 60, and 61 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to isolated polynucleotides encoding instant SEQ ID NO: 4 or a variety of variants and/or fragments of instant SEQ ID NO: 4 which have "chemokine activity" or which are "immunogenically active fragments." The claims further recite constructs comprising these nucleic acids, including vectors and host cells/organisms, as well as methods for producing polypeptides which utilize these constructs.

The specification teaches that instant SEQ ID NO: 3 encodes instant SEQ ID NO: 4, a polypeptide referred to in the specification as PANEC-2. The specification teaches that PANEC-2 is a human pancreatic protein that is a member of the C-C chemokine family, based on the fact that the molecule was isolated from a library obtained from human pancreatic tissue and based on homology of SEQ ID NO: 4 to other C-C chemokines.

The specification asserts that PANEC-2 is specifically expressed in pancreas, and because of this PANEC-2 nucleic acids are useful in assays based on chemokine production in cases of inflammation or disease affecting the pancreas (p. 8). While asserted utility is specific, it is not substantial. It is not substantial because further experimentation would be required to

reasonably confirm that in fact a real world utility exists wherein these molecules can be used in diagnostics.

Chemokines are chemoattractant cytokines. In a 1994 review of chemokines, Schall *et al.* teach that "Although the properties of these molecules have only recently begun to be elucidated, the bulk of the evidence to date suggests that the chemokines function as regulators of inflammatory and immunoregulatory processes, particularly through their leukocyte chemoattractant effects (p. 4, third paragraph, as cited in the IDS)." A "leukocyte" is a white blood cell, and includes among its members monocytes, neutrophils, basophils, eosinophils, and lymphocytes, each of which function differently within the body's immune system. Furthermore, Schall *et al.* provide a table which summarizes different sources and targets for the known C-C type chemokines (Table V). Some of these, for example MCP-1, can be isolated from many tissues, while others can be isolate from only T cells (for example I-309). Likewise, with regard to targets, some of the C-C type chemokines target a wide variety of cells, for example MIP-1α targets a variety of leukocytes as well as stem cells, osteoclasts, and hypothalamus. And for some the target is yet unknown, such as the murine C-C chemokine C10. Furthermore, Schall *et al.* teach that even chemokines with a great deal of structural homology (70%) demonstrate distinct specificities for their cellular targets (p. 16, first full paragraph), and that attempts to even elucidate the targets of chemokines contain "pitfalls of interpretation (p. 23, second paragraph)." The pancreas is a complex organ with many cell types- the specification does not provide any information as to what type of cells produce or are targeted by PANEC-2. Thus, in the instant case, while applicant may have identified a C-C type chemokine, this designation does not speak specifically to the functioning of the molecule with regard to target,

and further experimentation (which is unpredictable) would be required to determine such a target. Without knowledge of such a target, it would be difficult to utilize the instant molecule in diagnostics or prognostics because it is unknown what the presence of the molecule would indicate or suggest.

Furthermore, the instant specification asserts that the PANEC-2 molecule is "specifically" expressed in pancreas and can therefore be used in assays to detect diseases or inflammation of the pancreas. However, the specification does not provide any evidence of this specific expression, only teaching that the molecule was isolated from a human pancreatic cDNA library, but never assaying additional tissue types to determine the specificity of expression. Accordingly, the assertion that PANEC-2 is "specifically" expressed in the pancreas is not substantial. All that can be concluded based upon the specification as filed is that PANEC-2 is expressed in pancreas, not that such expression is specific to pancreas. Indeed, the post-filing date art suggests that the PANEC-2 molecule (SEQ ID NO: 4) is expressed in a wide variety of tissues, including lymph nodes, appendix, heart, small intestine, colon, and spleen (Nagira *et al.*, 1997, figure 3). This reference supports the position that at the time the invention was made further experimentation would have been necessary to even reasonable confirm the expression specificity of the instant molecule.

The specification does not elucidate or demonstrate any particular target for the instantly disclosed chemokine, but instead teaches that excessive expression of PANEC-2 "can" lead to activation of monocytes, macrophages, basophils, eosinophils, T lymphocytes, and/or other cells which respond to chemokines. The language of the specification appears to be prophetic, and suggests that PANEC-2 may activate any one of these or some other undisclosed molecule, but it

is equally suggestive that it may not activate any one of these. This is not a definitive assertion of functionality or utility. It is also noted that chemokines are particularly discussed in the specification at several citations regarding their broad activities. For example, on pages 2-3, various chemokines are described with varying activities discussed. Particular attention is drawn to page 3, line 9, wherein it is stated that chemokine activities demonstrate a high degree of target cell specificity. This statement is significant in that the subject matter of the instant claims is "not" characterized as target cell specificity other than the generic pancreas location thereof. Numerous activities are carried out by the pancreas, including numerous non-chemokine activities, and thus this pancreas specificity is generic in nature, especially since the chemokines encoded by the instantly claimed nucleic acids have no asserted correlation to any particular disease or illness, but rather only speculated as being involved in a long list of diseases or illnesses. Thus, the asserted utility of the claimed PANEC-2 encoding nucleic acids as a tool in diagnostics is not substantial because the specification does not teach or suggest the "inflammatory or disease" affecting the pancreas that can be identified using these molecules. Instead, the disclosure of the specification is an invitation to the skilled artisan to attempt to discover such a disease that is associated with the instantly claimed nucleic acids, and can thus be detected in a diagnostic which utilizes these nucleic acids. Thus, "real world" disease or illness condition correlation is absent for the claimed subject matter, and the asserted utility of the instant nucleic acids in diagnostic applications is not substantial.

The specification further asserts a number of additional possible utilities for the claimed nucleic acids, including as hybridization probes, as oligomers for PCR, use for chromosome and gene mapping, use in the recombinant production of PANEC-2, and use in the generation of anti-

sense DNA or RNA, their chemical analogs, and the like (p. 8, third full paragraph). These utilities are not specific because they can generally be applied to any nucleic acid that encodes a protein, of which there are millions of possibilities. Further, these utilities are not substantial. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the proteins that are to be produced as final products resulting from processes involving claimed nucleic acid have asserted or identified specific and substantial utilities. The research contemplated by applicants to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties a protein itself or the mechanisms in which the protein is involved does not define "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds.

Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compounds such that another non-asserted utility would be well established for the compounds. In the instant specification in the fourth full paragraph on page 4, applicants set forth a research proposal for "new diagnostic techniques" and for "use in the development of effective therapies." This statement in itself appears to be an

invitation to conduct further research to reasonably confirm that a specific and substantial utility exists for the claimed molecules. It is noted that a number of examples have been set forth for the basic isolation and characterization of PANEC-2 starting in the instant specification on pages 13-15. From pages 16-26 of the specification a review of generic methods are given with only speculation as to what specific or substantial effects are connected to PANEC-2. These are also clearly research proposals which lack patentable utility. In summary, the instant invention, as filed, has not been set forth with a patentable utility due to a lack of specific, substantial, or well established utility.

Claims 1-10, 12, 13, 60, and 61 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112-Written Description

14. Claims 3, 6, 7, 8, 9, 12, 13, 60, and 61 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Rejected claim 3 is drawn to isolated polynucleotides encoding a polypeptide comprising an amino acid sequence of SEQ ID NO: 4, or a polypeptide that is an allelic or recombinant variant of SEQ ID NO: 4, wherein said variant has an insertion or deletion of 1-5 amino acids as compared with SEQ ID NO: 4 and/or has one or more amino acid substitutions as compared with

SEQ ID NO: 4 and has the amino acid sequence of SEQ ID NO: 4 at a listing of particular amino acids of SEQ ID NO: 4 (see claim 1), wherein the variant has chemokine activity, or a biologically active fragment of a polypeptide having an amino acid sequence SEQ ID NO: 4, wherein said fragment has chemokine activity, or an immunogenically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO: 4, wherein said immunogenically active fragment is capable of generating an antibody that specifically binds to the polypeptide of SEQ ID NO: 4.

The genus of nucleic acids encompassed within this claim includes a wide variety of polynucleotides encoding amino acid sequences that are not described. For example, part (b)(iii) recites that the encoded variant has an insertion of 1-5 amino acids as compared to SEQ ID NO: 4. This recitation using the word "has" is open claim language, and so, while the language of the claim requires that the variant has 1-5 amino acid inserted or deleted, this requirement is a MINIMUM requirement as to the number of insertions or deletions permitted within the language of the claim. Furthermore, when this is combined with part (b)(ii) of the claim which requires certain amino acid residues to be present (note parts (iii) and (ii) are linked using and/or) it means that even part (ii) which recites the amino acid residues that must be present in the encoded polypeptide is permitted to have any number of deletions or insertions between the residues. Essentially this combination of permitted changes in the variants recited in claim 3(b) results in very little required structure of the encoded polypeptide relative to SEQ ID NO: 4. Furthermore, the claims do not recite a requisite structure/function relationship between a recited function in the claims and a function of the encoded amino acid. Though the claim recites that the encoded variant must have "chemokine activity" this recitation of function is very broad, as

chemokines are known to be active in a variety of ways, as proteins that bind to receptors that then transmit a wide variety of possible signals within a cell. There is no clear relationship between the structure recited in part (b) of the claim and the recited "function."

Considering part (c) the polynucleotide of claim 3, this genus of nucleic acids is also quite broad, because while the claim requires that the encoded fragment be "biologically active" and have "chemokine activity" this could include any number of possible amino acid residues. Since these two recited functions are broad in their nature (biological activity encompassing even an activity such as being a substrate for a protease or the ability to raise an antibody), these functions do not help to define the claimed genus. Furthermore, the specification does not discuss which fragments of SEQ ID NO: 4 are essential for the maintenance of "chemokine activity" a fact that is particularly relevant in view of the fact that the specification does not even demonstrate what type of chemokine activity SEQ ID NO: 4 possesses to begin with. Furthermore, the claim is open in nature, requiring only that the claimed polynucleotide encode a fragment of SEQ ID NO: 4 that meets the functional language of the claim, but that polynucleotide could further encode other fragments flanking the fragment of SEQ ID NO: 4, and so the claimed polynucleotide encompasses polynucleotides that encode related chemokines, allelic variants not disclosed, as well as possible splice variants of the disclosed nucleic acid.

Part (d) of claim 3 encompasses any nucleic acid encoding any immunogenically active fragment of SEQ ID NO: 4 wherein the fragment is "capable" of generating an antibody that "specifically binds" to SEQ ID NO: 4. The specification at page 12 teaches that antibodies inherently specifically bind their target as opposed to other target sequences, and so in this case, the language "specifically binds" is quite broad in nature and does not provide a defining

characteristic, as any antibody raised by a fragment of SEQ ID NO: 4 would specifically bind some portion of SEQ ID NO: 4. Furthermore, the claim is open in nature, requiring only that the claimed polynucleotide encode a fragment of SEQ ID NO: 4 that meets the functional language of the claim, but that polynucleotide could further encode other fragments flanking the fragment of SEQ ID NO: 4, and so the claimed polynucleotide encompasses polynucleotides that encode related chemokines, even polypeptides that are not chemokines but share some amino acid sequence in common with SEQ ID NO: 4, allelic variants not disclosed, as well as possible splice variants of the disclosed nucleic acid.

Claims 6-9 are drawn to constructs and methods that utilize or comprise nucleic acids of claim 3.

Claim 12 encompasses much of the same subject matter as claim 3(b), specifically reciting an isolated nucleic acid comprising instant SEQ ID NO: 3 or a naturally occurring polynucleotide sequence variant of SEQ ID NO: 3, wherein the variant encodes SEQ ID NO: 4, and differs from SEQ ID NO: 4. One significant difference in the scope of claim 3 and claim 12 is that the claim recites only "naturally occurring" polynucleotides, yet the specification does not describe how to identify out of the polynucleotide encompassed within the recitation of claim 12(b) which ones are "naturally" occurring. Neither the specification nor the claims describes any structural features of the claimed polynucleotides that would help to identify them as naturally occurring.

Claim 13 claims an isolated polynucleotide comprising at lest 60 contiguous nucleotides of a polynucleotide of claim 12, which is broader in scope than even claim 12 as it requires less

sequence to be present, and like claim 12 it uses open claim language which means the minimal 60 nucleotides can be flanked on either side by additional sequences.

Claims 60 and 61 are limited to be non-genomic sequences and sequences without introns. The still encompass a wide variety of possible variants as discussed herein.

Within the genus of the claimed polynucleotides, the instant specification describes only nucleic acids encoding SEQ ID NO: 4, with a particular example of a nucleic acid comprising instant SEQ ID NO: 3. Molecules that consist of fragments of SEQ ID NO: 3 are also described, as are molecules that encode amino acids sequences consisting of fragments of SEQ ID NO: 4. As discussed, however, the claims encompass any number of variants and sequences related to SEQ ID NO: 3 and encoding polypeptides related to SEQ ID NO: 4 that are not described in the specification. It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic sequence of the disclosed SEQ ID NO: 3 and encoding SEQ ID NO: 4 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids encoding proteins modified by addition, insertion, deletion, substitution or inversion with the disclosed SEQ ID No: 4 therefore possessing one or

more amino acid differences such that a different amino acid sequence is encoded which retains same function as SEQ ID NO: 4, which function is not clearly set forth in the specification.

Claim Rejections - 35 USC § 112, 2nd Paragraph

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 60, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 depends from claim 1 which recites in part (b) "a polypeptide encoding an allelic or recombinant variant." This language is indefinite because it is not clear what is meant by the recitation that the polypeptide encode a variant, as polypeptides are not generally considered to encode other molecules, but instead themselves are encoded by polynucleotides. Clarification is required. Claims 4-10 all depend from claim 3 and are indefinite over this recitation as well.

Claim 12 is indefinite in part (b) of the claim because this section of the claim recites a "naturally occurring polynucleotide variant of SEQ ID NO: 3" and then further recites "wherein said variant (i) differs by an insertion and or deletion of 1-5 amino acids as compared with SEQ ID NO: 4..." The claim is indefinite over these recitations because first the claim recites a variant of SEQ ID NO: 3, which is a nucleic acid sequence, and then the claim defines the variant in terms of a different sequence, that is SEQ ID NO: 4 an amino acid sequence. Claim 12 is further indefinite because it recites "an RNA equivalent of a)-d)," in the last line of the claim, yet the claim does not have parts (c) and (d). It appears that there is an error in the labeling of

the parts of the claim, and this error renders the claim indefinite. Claims 13, 60, and 61 all depend from claim 12 and are indefinite over these recitation as well.

Claim Objections

17. Claims 3, 4, 5, 6, 7, 8, 9, 10 are objected to because claim 1, from which these all depend, recites in part (b) three subsections numbered (iii), (ii), and (iii) and the use of two subsections with the same number is confusing. It appears that the first subsection (iii) would be more appropriately numbered (i). Correction is required.

18. Claims 12, 13, 60, and 61 are objected to because claim 12, from which claims 13, 60, and 61 depend, recites four different sections labeled as "ii." It appears that there is an error in the labeling of these sections. Correction is required.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 3, 6-9, 12, 13, 60, and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Caput *et al.* (WO 92/09629).

For applicant's convenience it is noted that the PCT application represented by this WO publication matured into a 371 application filed in the United States which issued as US 6001649. This US Patent provides an English language translation of the French PCT relied upon in this rejection.

Caput *et al.* teach an isolated polynucleotide encoding a polypeptide that is a polypeptide that is an allelic variant or recombinant variant of the amino acid sequence SEQ ID NO: 4, wherein said variant has an insertion or deletion of 1-5 amino acids as compared to SEQ ID NO: 4 and further wherein the variant has chemokine activity. The language of the instant claim is drawn using open claim language "has" and thus is interpreted to mean that the claim is meant to encompass any isolated nucleic acid encoding a polypeptide that is a variant of SEQ ID NO: 4 wherein said variant has an insertion or deletion of 1-5 amino acids relative to SEQ ID NO: 4, but can have any number of such insertions or deletions.

Caput *et al.* teach an isolated nucleic acid encoding a chemokine. The nucleic acid taught by Caput *et al.* encodes a chemokine that has an insertion of three amino acids between residues 27 and 28 of instant SEQ ID NO: 4 (see alignment below, Qy=SEQ ID NO: 4, Db= SEQ ID NO: 15 of Caput *et al.*), thus, the molecule "has" an insertion of three amino acids compared to SEQ ID NO: 4. It is noted that the molecule also contains a large number of additional insertions and deletions relative to SEQ ID NO: 4, for example, between the first and fourth amino acid residues of SEQ ID NO: 4 there is a deletion of the residues AlaGln and an insertion of residues LysAla. Alternately, this difference could be described as an insertion of a Lys after the first residue of SEQ ID NO: 4, and a deletion of Gln from the third residue of SEQ ID NO: 4. As the claim places no structural limits on the number of insertions or deletions permissible within the scope of the claim, and as the molecule encoded by the polynucleotide taught by Caput *et al.* encodes a cytokine, the reference is considered to teach the invention of claims 3 and 12.

Further, Caput *et al.* teach an isolated nucleic acid encoding a an immunogenically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO: 4 wherein said

immunogenically active fragment is capable of generating an antibody that specifically binds to the polypeptide of SEQ ID NO: 4. Caput *et al.* teach a polynucleotide that encodes residues 75-78 of SEQ ID NO: 4, and this four amino acid fragment would be immunogenically active, that is able to raise an antibody. The raised antibody would specifically bind to this portion of SEQ ID NO: 4. The specification at page 12 teaches that antibodies inherently specifically bind their target as opposed to other target sequences, and so in this case, the language "specifically binds" is quite broad in nature and essentially applies to any antibody that would bind a target sequence, as any antibody raised by a fragment of SEQ ID NO: 4 would specifically bind some portion of SEQ ID NO: 4. Thus, the nucleic acid taught by Caput *et al.* meets at least this additional aspect of claim 3.

With regard to claim 6, Caput *et al.* teach recombinant polynucleotides comprising a promoter sequence operably linked to their SEQ ID NO: 15 and, with regard to claims 7 and 8, they teach host cells which are transgenic organisms comprising the recombinant polynucleotides. With regard to claim 9, Caput *et al.* teach a method for producing the polypeptide encoded by their SEQ ID NO: 15, which comprises culturing a cell under conditions suitable for the expression of the polypeptide, and recovering the polypeptide (Sections 5-7, pages 31-44).

With regard to claim 13, polynucleotide taught by Caput *et al.* comprises more than 60 nucleotides.

With regard to claims 60 and 61, the cDNA taught by Caput *et al.* is not genomic, and it does not contain introns. These are inherent features of the molecule taught by Caput *et al.*

Thus, the teachings provided by Caput *et al.* meet all of the limitations of the rejected claims.

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Qy          1 MetAlaGlnSerLeuAlaLeuSerLeuLeuIleLeuValLeuAlaPheGlyIleProArg 20
              |||       |||    ||||||       |||:::|||       |||          |||:::
Db         71 ATGAAAGCCTCTGCAGCACTTCTGTGTCTGCTGCTCACAGCAGCTGCTTTCAGCCCCCAG 130

Qy         21 ThrGlnGlySerAspGlyGly---------AlaGlnAspCysCysLeuLysTyrSerGln 37
                              |||          :::       ||||||    ::::::
Db        131 GGGCTTGCTCAGCCAGTTGGGATTAATACTTCAACTACCTGCTGCTACAGATTTATCAAT 190

Qy         38 ArgLysIleProAlaLysValValArgSerTyrArgLysGlnGluProSerLeuGlyCys 57
              :::||||||||||    :::    :::    ||||||||||:::          |||       |||
Db        191 AAGAAAATCCCTAAGCAGAGGCTGGAGAGCTACAGAAGGACCACCAGTAGC---CACTGT 247

Qy         58 SerIleProAlaIleLeuPheLeuProArgLysArgSerGlnAlaGluLeuCysAlaAsp 77
                       |||::::::::|||       :::    :::          |||:::|||||||||
Db        248 CCCCGGGAAGCTGTAATCTTC------AAGACCAAACTGGACAAGGAGATCTGTGCTGAC 301

Qy         78 ProLysGluLeuTrpValGlnGlnLeuMetGlnHisLeuAsp---LysThrProSerPro 96
              |||    :::    |||||||||       |||:::||||||||||    ||||||    :::|||
Db        302 CCCACACAGAAGTGGGTCCAGGACTTTATGAAGCACCTGGACAAGAAAACCCAAACTCCA 361

Qy         97 Gln 97
              :::
Db        362 AAG 364
```

Conclusion

21. Applicant's comments regarding the prior art cited in the previous office action and a potential interference have been noted. The comments regarding the prior art (much of which is not in fact "prior" relative to the effective filing date of this application) have been reviewed. Regarding a possible interference, these comments are not timely filed, as the question of a possible interference will not be taken up for consideration until there is a finding of an allowable claim. As of the writing of this office action, no such claim exists. When such a claim is presented and agreed upon by the examiner, Applicant's comments regarding a possible interference will be carefully considered.

22. No claims are allowed.

23. Claim 4, 5, and 10 are free of the prior art. The prior art does not teach or suggest an isolated polynucleotide encoding SEQ ID NO: 4, and in particular does not teach an isolated polynucleotide comprising instant SEQ ID NO: 3.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM. Please note on January 14, 2003 the examiner's telephone number will change to (571) 272-0753.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached by calling (703) 308-1119. Beginning January 14, 2003 Gary Benzion's telephone number will be (571) 272-0782.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C Switzer
Examiner
Art Unit 1634

February 20, 2004

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